ORAL CONTRIBUTIONS

854 Cardiomyopathy: Diabetes, Collagen, Bundle Branch Block, BNP, and Muscular Dystrophy

Tuesday, March 19, 2002, 10:30 a.m.-Noon
Georgia World Congress Center, Room 255W

10:30 a.m.

854-1 High Prevalence of Impaired Glucose Metabolism in Patients With Idiopathic Dilated Cardiomyopathy

Aamer H. Jamali, Ronald M. Witteles, W. H. Wilson Tang, James W. Chu, Gerald M. Reaven, Michael B. Fowler, *Stanford University School of Medicine, Stanford, California.*

Background: The pathogenesis of idiopathic dilated cardiomyopathy (IDC) is poorly understood. Reversible metabolic derangements such as insulin resistance (IR) have recently been described as potential causes of reduced contractility. Indeed, treatment of IR has been shown to slow the progression of systolic dysfunction in animal models. Because patients with IR have a high frequency of impaired glucose metabolism, we sought to establish the prevalence of impaired glucose metabolism in IDC.
Methods: The records of 230 consecutive medically stable outpatients referred for transplant evaluation to the Stanford University Cardiomyopathy Clinic were reviewed, of which 104 had IDC. Twenty of these patients had diabetes mellitus (DM) and were excluded from further testing. Forty-one patients were unable to be contacted or declined testing. The remaining 43 patients underwent fasting metabolic measurements and oral glucose tolerance testing.
Results: Of the 43 patients tested, 21 (49%) exhibited impaired glucose metabolism, manifested by either impaired glucose tolerance (n=12), impaired fasting glucose (n=3), or previously undiagnosed DM (n=6) as defined by the American Diabetes Association. There were no significant differences in age, gender, race, heart failure class, family history of DM, body mass index, or history of hypertension between the patient groups.
Conclusions: This study demonstrates a strikingly high prevalence of impaired glucose metabolism in non-DM patients with IDC, in addition to a high prevalence of previously diagnosed DM. Patients with occult glucose dysmetabolism could not be distinguished on the basis of historical details or anthropometric measurements. These patients may comprise a subgroup in which disease progression can be delayed or reversed by correction of the metabolic derangement. Thus, our group recommends the routine testing of all patients with IDC for impaired glucose metabolism.

10:45 a.m.

854-2 Carvedilol Is More Potent Than Candesartan in the Treatment of Cardiac Dysfunction From Diabetes

Tetsuya Hayashi, Tatsuhiko Mori, Sakiko Endo, Hiroaki Shimomura, Koichi Sohmiya, Yasushi Kitaura, *Osaka Medical College, Takatsuki, Japan.*

Oxidative stress in diabetes might contribute to cardiomyocyte dysfunction and induce the stress protein heme oxygenase (HO)-1. The OLETF (Otsuka Long-Evans Tokushima Fatty) rats at 40 weeks of age (n=40), exhibiting non-insulin dependent diabetes mellitus, were divided into three groups and treated with candesartan 0.2 mg/kg/day (ARB), carvedilol 10 mg/kg/day (B) or vehicle (V) for 4 weeks. In all animals, including control LETO rats (n=20), ultrastructure and HO-1 in the myocardium and TBARS (thiobarbituric acid-reactive substances) in the plasma were studied. The OLETF rats caused left ventricular (LV) dysfunction, severe myocardial degeneration, and increased HO-1 and TBARS, compared to LETO rats. Though LV dysfunction was improved by either treatment, histological changes were minimal and oxidative stress was significantly reduced only in rats with B (Table). Conclusion: Carvedilol was more potent for reduction of oxidative stress, and was more protective for heart than candesartan. Thus, reduction of oxidative stress should be the major target in the treatment of cardiac dysfunction from diabetes.

Table. Summary of Hemodynamic Data and TBARS

	Hw/Bw	HR	LVsys	LVed	max dP/dt	min dP/dt	TBARS
L	2.5+/-0.1	402+/-40	96+/-4	6+/-2	3496+/-750	3543+/-285	2.9+/-0.6
O+V	2.8+/-0.3	259+/-64*	113+/-7*	11+/-2*	2941+/-269	2358+/-224*	8.2+/-1.9*
O+ARB	2.5+/-0.1	294+/-53	77+/-5**	7+/-2**	3240+/-746	3420+/-746**	7.6+/-1.3
O+B	2.5+/-0.1	211+/-17	119+/-8*	7+/-2**	4275+/-512**	4275+/-512**	4.8+/-1.2**

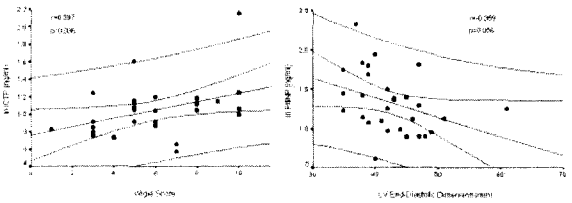
L; LETO, O+V; OLETF+vehicle, O+ARB; given candesartan, O+B; given carvedilol, Hw/Bw; heart/body weight ratio (mg/g), HR; heart rate (bpm), LVsys and LVed; LV systolic and end-diastolic pressure (mmHg), max and min dP/dt; peak positive and negative dP/dt (mmHg/sec), TBARS; nM/ml. Values are mean +/- SD. *p<0.05 vs. LETO, **p<0.05 vs. OLETF.

11:00 a.m.

854-3 Myocardial Collagen Turnover in Hypertrophic Cardiomyopathy: Comparison to Healthy Subjects

Raffaella Lombardi, Sandro Betocchi, Maria Angela Losi, Quirino Ciampi, Carlo G. Tocchetti, Elpidio Pezzella, Filippo Finizio, Mariano Aversa, Marianna Miranda, Veronica De Crescenzo, Massimo Chiariello, *Department of Clinical Medicine, Cardivascular and Immunological Science, University of Naples, Naples, Italy.*

BACKGROUND LV hypertrophy and fibrosis are characteristics of hypertrophic cardiomyopathy (HCM). We assessed the impact of collagen turnover on LV anatomy and function in HCM. METHODS We studied 29 HCM patients (36±9 years) and 10 age and sex-matched controls. We assessed cardiac fibrosis by RIA measurement of serum concentrations of: procollagen III N-terminal propeptide (PIIINP), index of collagen III synthesis; procollagen I C-terminal propeptide (PICP) and collagen I C-terminal telopeptide (ICTP), indexes of collagen I synthesis and degradation. They were ln-transformed. LV hypertrophy was quantified by the Wigle's score. Diastolic function was evaluated by the duration difference in antegrade (mitral) and retrograde (pulmonary vein) A wave (Adiff). RESULTS PIIINP and ICTP were higher in HCM than in controls (1.3(.4) vs .9(.3) ng/ml, p=.002; 1.0(.4) vs .8(.2) ng/ml, p=.048) and inversely related to age in HCM (r=-.424, p=.022; r=-.651, p<.001). PICP and ICTP were directly related to one another (r=.395, p=.013). PIIINP was inversely related to LV end-diastolic dimension, while ICTP was directly related to Wigle's score (Figure). PIIINP and ICTP were inversely related to Adiff (r=-.393, p=.035; and r=-.584, p<.001). CONCLUSIONS In HCM patients collagen metabolism is more active than in controls and it decreases with age. Collagen I degradation parallels synthesis (steady state). Collagen turnover influences degree of hypertrophy, cavity size and passive diastolic properties.



11:15 a.m.

854-4 Does Isolated Bundle Branch Block Cause Left Ventricular Remodeling?

Seung-Joon Lee, Eric J. Putz, Elyse Foster, Teresa DeMarco, Leslie A. Saxon, *University of California San Francisco, San Francisco, California.*

Background: Population studies have identified the presence of bundle branch block (BBB) as an independent risk factor for total mortality in pts with known cardiac disease. It is unknown how chronic ventricular dyssynchrony resulting solely from conduction delay impacts ventricular function. We performed a retrospective pilot study to determine if chronic, isolated BBB affects echocardiographic measures of progressive ventricular remodeling.
Methods: Patients were consecutively identified from the UCSF ECG database with QRS duration >=120ms. Retrospective chart review was conducted in 126 pts (age=71.9±16.5 yrs; Female=49%). Pts were excluded based on presence of coexisting heart disease. Those pts with isolated BBB and without identifiable cardiac disease who had serial echocardiograms for comparison comprised the study population.
Results: Of 126 pts with QRS>=120ms, 69 pts (55%) had coexisting cardiac disease versus 57 (45%) without identifiable cardiac disease. Of the 57 pts, 22 (39%) pts had sequential measures of left ventricular (LV) function available for review (Table). LV ejection fraction (LVEF) was reduced by 19.5% in the isolated LBBB cohort (p=0.0125) versus 3.1% reduction in isolated RBBB cohort (p=0.4106).
Conclusion: In a subset of pts, LBBB often precedes LV remodeling. Our pilot data suggests isolated LBBB may be the earliest manifestation of a progressive subclinical cardiomyopathic process and BBB induced LV dyssynchrony may itself trigger ventricular remodeling.

	No LVEF change (%)	Reduction in LVEF (%)	Mean F/U (months)
All pts n=22	14 (64%)	8 (36%)	64.1±50.8
LBBB n=12	5 (42%)	7 (58%)	55.8±36.96
RBBB n=10	9 (90%)	1 (10%)	73.9±64.4